REMARKS

Applicants thank the Examiner for the very thorough consideration given the present application.

Claims 1-12 are now present in this application. Claims 1, 2, 11 and 12 are independent. By this Amendment, claims 1-5 and 8-11 are amended, and claim 12 is added. No new matter is involved.

Reconsideration of this application, as amended, is respectfully requested.

Personal Interview

Applicants acknowledge with appreciation the courtesies extended by Examiners David. C. Mellon and Tony G. Soohoo to their representative, Mr. Robert J. Webster, Reg. No. 46,472 during the personal interview conducted on January 8, 2010. During that interview, Applicants' representative argued that the restriction requirement was improper and should be withdrawn, and the patentability of the independent claims was discussed. No agreement was reached on those issues. The Examiners and Applicants' representative discussed possible claim language in an attempt to reach agreement on claim language that patentability defines over the applied art. The claim amendments reflect those discussions.

Restriction Requirement

The Examiner has made the holding of lack of unity of invention/restriction requirement final, and has withdrawn claims 9 and 10 from further consideration.

Applicant continues to traverse the holding of lack of unity of invention/restriction

requirement for the following reasons.

37 CFR §1.475(b), which applies to this Application, clearly, unequivocally and unmistakably states, in pertinent part, that a national stage application containing claims to different categories of invention *will be considered to have unity of invention* if the claims are drawn to only one of the following categories: (1) A product and a process specially adapted for the manufacture of said product.

The Office is bound to follow its own rules of practice, including this specific Rule of Practice during this national stage of Applicant's PCT Application.

Applicant respectfully submits that claims 9 and 10 are processes specially adapted for the manufacture of the product recited in claim 1 (and claim 2 with respect to claim 9).

In reply, the Office Action states that none of the method of manufacture steps are in fact specially adapted to the product at this time but, rather, are generic manufacturing claims to hollow fiber membrane assemblies.

Applicants respectfully disagree for the following reasons.

Firstly, the PCT Administrative Instructions found in Annex B (Section AI of the MPEP), clearly state that a process shall be considered to be specially adapted for the manufacture of a product if the process inherently results in the claimed product with the technical relationship being presently between the claimed product and the claimed product, and "[T]he words 'specially adapted' are not intended to imply that the product could not also be manufactured by a different process."

Applicants respectfully submit that the processes recited in claims 8 and 9 inherently result the claimed product because claims 8 and 9 clearly recite "a method for manufacturing

the external pressure type hollow type fiber membrane module according to claim 1 or claim 2." Accordingly, claims 8 and 9 processes which are specially adapted for the manufacture of the products of claims 8 and 9, respectively.

Accordingly, the Office is required to examine all pending claims, including claims 9 and 10.

Thus, withdrawal of the restriction requirement/lack of unity of invention holding, and reinstatement and examination of claims 9 and 10 along with claims 1-8 are respectfully requested.

Entry of Amendments

Applicants respectfully submit that because a new, non-final Office Action will have to be made with respect to claims 8 and 9, it is proper to enter the claim amendments presented above.

Rejection Under 35 U.S.C. § 102

Claims 1, 2 and 11 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Re. 36,125 to Haworth et al. ("Haworth"). This rejection is respectfully traversed.

A complete discussion of the Examiner's rejection is set forth in the Office Action, and is not being repeated here.

A prior art reference anticipates the subject matter of a claim when that reference discloses every feature of the claimed invention, either explicitly or inherently. *In re Schreiber*, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997) and *Hazani v. Int'l Trade Comm'n*, 126 F.3d 1473. 1477. 44 USPQ2d 1358, 1361 (Fed Cir. 1997). While, of course, it is possible that it is inherent in the operation of the prior art device that a particular element operates as theorized by the

Examiner, inherency may not be established by probabilities or possibilities. What is *inherent*, must necessarily be disclosed. *See In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981); *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

During patent examination the PTO bears the initial burden of presenting a *prima facie* case of unpatentability. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet this burden, then the applicant is entitled to the patent. However, when a *prima facie* case is made, the burden shifts to the applicant to come forward with evidence and/or argument supporting patentability. Patentability *vel non* is then determined on the entirety of the record, by a preponderance of evidence and weight of argument, *In re Gulag*, 62 USPQ2d 1151 (Fed. Cir. 2002).

Moreover, as stated in MPEP §707.07(d), where a claim is refused for any reason relating to the merits thereof it should be "rejected" and the ground of rejection fully and clearly stated.

Additionally, findings of fact and conclusions of law by the USPTO must be made in accordance with the Administrative Procedure Act, 5 U.S.C. §706(A), (E) (1994). *See Zurko v. Dickinson*, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999).

A claim limitation is inherent in the prior art if it is necessarily present in the prior art, not merely probably or possibly present. *See Rosco v. Mirro Lite*, 304 F.3d 1373, 1380, 64 USPQ2d 1676 (Fed. Cir. 2002). The dispositive question regarding anticipation is whether one skilled in the art would reasonably understand or infer from the prior reference's teaching that every claim feature or limitation was disclosed in that single reference, *Dayco Products, Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1368, 66 USPQ2d 1801 (Fed. Cir. 2003).

Claim 1, as amended, recites an external pressure type hollow fiber membrane module comprising: a hollow fiber membrane bundle formed of a plurality of hollow fiber membranes, a cylindrical housing, and a nozzle for allowing a fluid to enter into and exit from the housing, the hollow fiber membranes being fixedly adhered to each other and to the inner wall of the housing at ends of the hollow fiber membrane bundle; a hollow part opened in one side or both sides of adheringly-fixed ends of the hollow fiber membrane; and wherein the nozzle for allowing the fluid to enter and exit therefrom is installed on a side face of the housing of at least one adheringly fixed end at which the hollow part is opened; wherein the membrane bundle has a cross-sectional area coincident with the cross-sectional area of the cylindrical housing and a ratio PB/PA of membrane-occupying rates is 0.50 or more but 0.95 or less when PA is defined as the membrane-occupying rate in a neighboring region (A) having a cross-sectional area that extends substantially symmetrically about a line coincident with the longitudinal axis of the nozzle and substantially bisecting the cylindrical housing and extends from a side of the cylindrical housing adjacent to the nozzle a substantial distance toward the center of the cylinder, and PB is defined as the membrane-occupying rate in a non-neighboring region (B) of the nozzle which has a cross-sectional area that extends from the neighboring region (A) up to a side face of the cylinder opposite to the side face of the cylinder where the nozzle is located among a membrane chargeable region in the inner side of an adheringly-fixed part, in at least one adheringly fixed end of the opened hollow part in the vicinity of the nozzle, and wherein the membrane occupying rate decreases along said coincident line from the nozzle to a side of the cylindrical housing opposite the nozzle

Claim 2, as amended, recites an external pressure type hollow fiber membrane module

comprising: a hollow fiber cartridge having a hollow fiber membrane bundle formed of a plurality of hollow fiber membranes, of which both end parts are adheringly fixed and hollow parts in at least one end of adheringly-fixed ends are opened; and a cylindrical housing accommodating the cartridge and having a nozzle for allowing a fluid to enter and exit therefrom installed on at least one side face, in which the nozzle installed is fixed so as to be placed in the vicinity of the inner surface of an adheringly-fixed part in the opened hollow parts side in the hollow fiber membrane cartridge; wherein the membrane bundle has a cross-sectional area coincident with the cross-sectional area of the cylindrical housing and a ratio PB/PA of membrane-occupying rates is 0.50 or more but 0.95 or less when PA is defined as the membrane-occupying rate in a neighboring region (A) having a cross-sectional area that extends substantially symmetrically about a line coincident with the longitudinal axis and substantially bisecting the cylindrical housing and extends from a side of the cylindrical housing adjacent to the nozzle a substantial distance from adjacent to the nozzle and toward the center of the cylinder, and PB is defined as the membrane-occupying rate in a non-neighboring region (B) of the nozzle which has a cross-sectional area that extends from the neighboring region (A) up to a side face of the cylinder opposite to the side face of the cylinder where the nozzle is located among a membrane chargeable region in the inner side of the adheringly-fixed part, in an adheringly-fixed end in the vicinity of the nozzle, and wherein the membrane occupying rate decreases along said coincident line from the nozzle to a side of the cylindrical housing opposite to the nozzle.

Claim 11, as amended, recites an external pressure type hollow fiber membrane module comprising: a cylindrical housing; a hollow fiber membrane bundle formed of a plurality of

hollow fiber membranes located inside of the cylindrical housing; a nozzle for allowing a fluid to enter into and exit from the housing, located on a side wall of the cylindrical housing wherein the membrane bundle is separated in cross-section into two regions, a first region taking up at least one fourth of the cross-sectional area of the membrane bundle located between a portion of the wall of the cylinder that extends about the nozzle to approximately the center of the cylinder, and a second region that extends from the first region to the side of the wall of the cylinder that is opposite to the side of the wall in which the nozzle is located, and wherein a ratio PB/PA of membrane-occupying rates is 0.50 or more but 0.95 or less when PA is defined as the membrane-occupying rate in the first region, and PB is defined as the membrane-occupying rate in the second region, and wherein the membrane occupying rate decreases across the two regions from the nozzle to a side of the cylindrical housing opposite to the nozzle.

With respect to claims 1 and 2, Applicants respectfully submit that Haworth's annular cross-sectional shaped hollow fiber bundle does not have a cross-sectional area coincident with the cross-sectional area of the cylindrical housing. The cross-sectional area of the cylindrical housing is a rod or disc, not an annulus.

Nor does Haworth disclose a neighboring region (A) having a cross-sectional area that extends substantially symmetrically about a line coincident with the longitudinal axis and substantially bisecting the cylindrical housing and extends from a side of the cylindrical housing adjacent to the nozzle a substantial distance from adjacent to the nozzle and toward the center of the cylinder, and a non-neighboring region (B) of the nozzle which has a cross-sectional area that extends from the neighboring region (A) up to a side face of the cylinder opposite to the side face of the cylinder where the nozzle is located among a membrane chargeable region in the

inner side of the adheringly-fixed part, in an adheringly-fixed end in the vicinity of the nozzle.

Nor does Haworth disclose a membrane occupying rate that decreases along said coincident line from the nozzle to a side of the cylindrical housing opposite to the nozzle.

With respect to claim 11, Haworth does not disclose a rod-shaped membrane bundle, but discloses a membrane bundle with an annular cross-sectional shape.

Further with respect to claim 11, Haworth does not disclose the membrane bundle is separated in cross-section into two regions, a first region taking up at least one fourth of the cross-sectional area of the membrane bundle located between a portion of the wall of the cylinder that extends about the nozzle to approximately the center of the cylinder, and a second region that extends from the first region to the side of the wall of the cylinder that is opposite to the side of the wall in which the nozzle is located, and wherein a ratio PB/PA of membrane-occupying rates is 0.50 or more but 0.95 or less when PA is defined as the membrane-occupying rate in the first region, and PB is defined as the membrane-occupying rate in the second region/

Furthermore, Haworth does not disclose a membrane occupying rate that decreases along from the nozzle to a side of the cylindrical housing opposite to the nozzle.

Furthermore, with respect to all recited claims, Applicant also respectfully submits that, significantly, Haworth does not disclose an external pressure type hollow fiber membrane module, as claimed. In this regard, it is Applicant's understanding that the driving force for the movement of oxygen from one side of a membrane into the other side, which is in contact with blood that needs to be oxygenated is the difference between the partial pressures of the oxygen in the blood and on the other side of the membrane. In Haworth, it appears that the partial pressure of oxygen that is supplied to the oxygenator unit is greater than the partial pressure of oxygen in

the blood that is supplied to the oxygenator unit, so that the oxygen will move from the inside of the microfibers to the blood that is on the outside of the microfiber (ref. col. 8, lines 8 to 14). See, in this regard, a four page article entitled, "Heparin-Coated Blood Oxygenators" with the following Internet citation: "http://biomed.brown.edu/Courses/BI108/2006-108websites/group01Heparin-coatedOxygen . . .," which describes how oxygenators like that of Haworth operate. A copy is attached for the Examiner's convenience.

Applicant also notes that one of ordinary skill in the art readily understands what is meant by an external pressure type of filtration system. In this regard, Applicant respectfully directs the attention of the Examiner to U.S. Patent 6,331,248 to Taniguchi et al., which explains, in col. 11, lines 45-54 the difference between an internal pressure filtration system and an external pressure filtration system. According to Taniguchi et al., in an external pressure type of hollow fiber membrane, the raw water is fed to the hollow portion of the hollow fiber membrane and filtration is effected from the inner surface side to the outer surface side of the membrane, whereas in an external pressure filtration system, the raw water is fed from the outer surface to the inner side surface of the membrane.

Accordingly, Haworth cannot possibly anticipate the claimed invention, which recites an external pressure type hollow fiber membrane module.

Thus, claims 1, 2 and 11 as amended, are not anticipated by Haworth.

Reconsideration and withdrawal of this rejection of claims 1, 2 and 11 are respectfully requested.

Rejections under 35 U.S.C. §103

Claims 1-5 and 11 stand rejected under 35 USC § 103(a) as being unpatentable over U.S. Patent Application Publication 2002/0079260 to Boivin et al. ("Boivin") in view of Haworth. This rejection is respectfully traversed.

A complete discussion of the Examiner's rejection is set forth in the Office Action, and is not being repeated here.

Because the rejection is based on 35 U.S.C. §103, what is in issue in such a rejection is "the invention as a whole, "not just a few features of the claimed invention. Under 35 U.S.C. §103, " [a] patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter *as a whole* would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." The determination under §103 is whether the claimed invention *as a whole* would have been obvious to a person of ordinary skill in the art at the time the invention was made. *See In re O'Farrell*, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). In determining obviousness, the invention must be considered as a whole and the claims must be considered in their entirety. *See Medtronic, Inc. v. Cardiac Pacemakers. Inc.*, 721 F.2d 1563, 1567, 220 USPQ 97, 101 (Fed. Cir. 1983).

In rejecting claims under 35 U.S.C. §103, it is incumbent on the Examiner to establish a factual basis to support the legal conclusion of obviousness. *See In re Fine*, 837 F.2d 1071, 1073, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). In so doing, the Examiner is expected to make the factual determinations set forth in *Graham v John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), and to provide a reason why one of ordinary skill in the pertinent art would have

been led to modify the prior art or to combine prior art references to arrive at the claimed invention. Such reason must stem from some teaching, suggestion or implication in the prior art as a whole or knowledge generally available to one having ordinary skill in the art. *See Uniroyal Inc. v. F-Wiley Corp.*, 837 F.2d 1044, 1051, 5 USPQ2d 1434, 1438 (Fed. Cir. 1988), *cert. denied,* 488 U.S. 825 (1988); *Ashland Oil, Inc. v Delta Resins & Refactories, Inc.*, 776 F.2d 281, 293, 227 USPQ 657, 664 (Fed. Cir. 1985), *cert. denied*, 475 U.S. 1017 (1986); *ACS Hospital Systems, Inc. v Montefiore Hospital*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). These showings by the Examiner are an essential part of complying with the burden of presenting a prima facie case of obviousness. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. *See In re Fritch*, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1783 84 (Fed. Cir. 1992). To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be suggested or taught by the prior art. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1970). All words in a claim must be considered in judging the patentability of that claim against the prior art. *See In re Wilson,* 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

A suggestion, teaching, or motivation to combine the prior art references is an "essential evidentiary component of an obviousness holding." *See C.R. Bard, Inc. v. M3 Sys. Inc.,* 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998). This showing must be clear and particular, and broad conclusory statements about the teaching of multiple references, standing alone, are not "evidence." *See In re Dembiczak*, 175 F.3d 994 at 1000, 50 USPQ2d 1614 at 1617 (Fed. Cir.

1999).

Moreover, it is well settled that the Office must provide objective evidence of the basis used in a prior art rejection. A factual inquiry whether to modify a reference must be based on objective evidence of record, not merely conclusory statements of the Examiner. *See In re Lee*, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002).

Furthermore, during patent examination, the PTO bears the initial burden of presenting a *prima facie* case of unpatentability. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785788 (Fed. Cir. 1984). If the PTO fails to meet this burden, then the Applicant is entitled to the patent. Only when a *prima facie* case is made, the burden shifts to the applicant to come forward to rebut such a case.

Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness:" *In re Kahn*, 441 F.3d 977,988(Fed. Cir. 2006) (quoted with approval in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

In the sentence just prior to citing the *Kahn* case, the U.S. Supreme Court clearly stated that there has to be an apparent reason to combine the known elements in the manner claimed. The Office has the burden of making out a *prima facie* case of obviousness, i.e., by presenting objective factual evidence of a reason to combine the known elements in the manner claimed. The *KSR* decision did not lift that burden from the Office.

The articulated reasoning has to express a rationale explaining what would have led an ordinarily skilled artisan to combine selected features from each reference in a way that would have resulted in the claimed invention. See, *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1741 (2007).

Thus, the Supreme Court reaffirmed the fundamental principles set forth in the *Graham v. John Deere Co.* decision, cited and discussed above.

Applicant respectfully submits that claims 1 and 2, as amended, patentably define over both Boivin and Haworth.

Boivin differs fundamentally from the claimed invention in that Bovin's bundle of fibers has annular zones of fibers of different density, the more densely packed fibers being on the outside annular regions of the bundle and the less densely fibers being located toward the center of the bundle. As shown in Fig. 5, for example, the density of the fibers peaks at the outside of the bundle and is minimal at the center of the bundle.

However, this is not what is claimed. In the claimed invention, the density of the fibers changes from a relative high density on the side of the bundle adjacent the side nozzle to a relatively low density on the side of the bundle opposite to the side adjacent to the side nozzle.

Moreover, Haworth and Boivin are used for different purposes and have different operational configurations, Boivin's devices being limited to a rod-shaped cross-section and being used as blood dialyzers where the blood is injected via a side wall inlet and removed via another side wall outlet, whereas Haworth's device is limited to blood oxygenation devices utilizing annular cross-section fiber bundles to accommodate the oxygenating gas.

Moreover, the Office Action does not establish whether Boivin's device is an external pressure type hollow fiber filter, and for reasons discussed above, Haworth's device is not an external pressure type hollow fiber filter. Accordingly, the conclusion that Boivin and Haworth are combinable because they are concerned with the field of varied packing fraction hollow fiber membranes is clearly undercut because it clearly overlooks the fact that the Office Action does

not establish whether Boivin's device is an external pressure type hollow fiber filter, and for reasons discussed above, Haworth's device is not an external pressure type hollow fiber filter.

If Boivin's device is an internal pressure type filter, then both Boivin and Haworth are not relevant to the claims, and if Boivin is an external pressure type filter, then the Office Action fails to explain what Haworth's internal pressure type filter has to do with properly modifying Boivin's external pressure type filter.

Additionally, the varied packing ratio configurations of both references differ significantly and the Office Action fails to explain exactly how Haworth's varied packing ratio configurations can be applied to Boivin's concentric packing ratio configurations to arrive at the claimed invention. Instead, the Office Action merely speculates that the configurations of Haworth (which Applicants note vary considerably) when applied to Boivin's concentric configuration will result in the claimed invention. Applicants respectfully disagree with this speculative conclusion, especially where the result of the proposed modification of Boivin will completely change its concentric configuration to a linear gradient from one side of Boivin's hollow chamber to san opposite side thereof, which will destroy Boivin's preferred embodiment (shown in Fog. 5).

Thus, the Office Action does not satisfactorily establish that one of ordinary skill in the art would be properly motivated to turn to Haworth to modify Boivin, as suggested.

Furthermore, Applicant respectfully submits that neither Boivin nor Haworth discloses or suggests the claimed invention no matter how they are combined.

Accordingly, reconsideration and withdrawal of this rejection of claims 1-5 and 11 are respectfully requested.

Claims 6 and 7 stand rejected under 35 USC §103(a) as being unpatentable over Boivin in view of Haworth and further in view of JP 62-204804 to Misao.

As noted above, Applicant respectfully submits that claims 1 and 2, from which claims 6 and 7 depend (in the alternative) is not rendered obvious by Boivin and Haworth. Moreover, Misao is not being applied to remedy the aforenoted deficiencies of the Boivin-Haworth reference combination with respect to claims 1 and 2. So, even if one of ordinary skill in the art were properly motivated to modify the Boivin-Haworth reference combination in view of Misao, as suggested, the so-modified version of Boivin-Haworth would not render obvious the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection of claims 6 and 7 are respectfully requested.

Claim 8 stand rejected under 235 USC §103(a) as being unpatentable over Boivin in view of Haworth and further in view of U.S. patent 5,282,966 to Walker.

As noted above, Applicant respectfully submits that claims 1 and 2, from which claim 8 depends (in the alternative) is not rendered obvious by Boivin and Haworth. Moreover, Walker is not being applied to remedy the aforenoted deficiencies of the Boivin-Haworth reference combination with respect to claims 1 and 2. So, even if one of ordinary skill in the art were properly motivated to modify the Boivin-Haworth reference combination in view of Walker, as suggested, the so-modified version of Boivin-Haworth would not render obvious the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection of claim 8 are respectfully requested.

Claim 12

New, independent claim 12 recites a combination of features which is not disclosed or made obvious by the prior art of record, including a rod-shaped bundle of hollow fiber membranes that has a has a neighboring region (A) having a cross-sectional area that surrounds the nozzle and extends from the nozzle approximately half way to a side of the cylindrical housing opposite to the nozzle, and a non-neighboring region (B) of the nozzle which has a cross-sectional area that encompasses the cross-sectional area of the cylindrical housing other than that cross-sectional area encompassed by neighboring region (A), and wherein the membrane occupying rate decreases along a line coincident with the longitudinal axis of the nozzle that substantially bisects the cylindrical housing from the nozzle to a side of the cylindrical housing opposite the nozzle.

Consideration and allowance of claim 12 are respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone Robert J. Webster, Registration No. 46, 472, at (703) 205-8000, in the Washington, D.C. area.

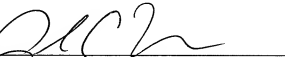
Prompt and favorable consideration of this Amendment is respectfully requested.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Date: MAR 1 2010

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By: 
Paul C. Lewis
Reg. No.: 43,368
P.O. Box 747
Falls Church, Virginia 22040-0747
Telephone: (703)205-8000

PCL/RJW:mmi:jmc

Attachment: Heparin-Coated Blood Oxygenators – four pages, as cited above

BROWN

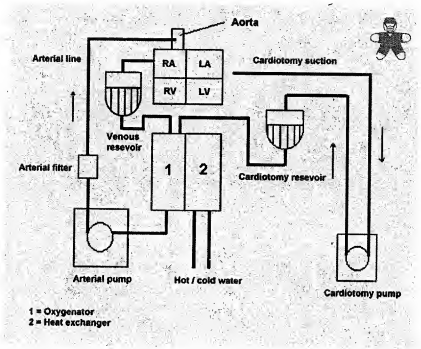
HEPARIN-COATED BLOOD OXYGENATORS

Oxygenator Basics

For most bypass graft operations such as CABG- Coronary artery bypass surgery, the cardiopulmonary bypass is undergone with the use of a heart-lung machine (or cardiopulmonary bypass machine). The heart-lung machine serves to replace the work of the heart during the open bypass surgery [2]. The machine replaces both the heart's pumping action, and adds oxygen to the blood. Since the heart is stopped during the operation, this permits the surgeon to operate on a bloodless, stationary heart. [3]

Procedures that use the heart-lung machine include :

- Coronary bypasses
- Heart transplants
- Removal and replacement of damaged valves
- Repair of other structural defects

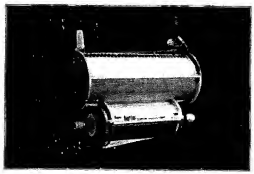


Click on the image above to see a short video of a perfusionist team at work.

The heart-lung machine is run by trained technicians otherwise known as perfusion technologists. Perfusion technologists are needed during surgery to run the machine. Normal surgical procedures with the use of the machine can take up to several hours. [2]

One component of the heart-lung machine is the oxygenator. The oxygenator component serves as the lung, and is designed to expose the blood to oxygen. It is disposable, and contains about 2-4 meters squared of membrane which is permeable to gas but impermeable to liquid blood. [4] Blood flows on one side of the membrane while oxygen on the other. The rate of oxygen addition is similar to that of normal respiration. Blood flow in an oxygenator is 3-5 liters/min and gas flow is between 40-60% of blood flow. [5] The oxygen partial pressure is around 65%. [6] Carbon dioxide is added to the sweep stream to maintain the proper blood gas level. As the blood passes through the oxygenator, the blood comes into intimate contact with the fine surfaces of the device itself. Oxygen gas is delivered to the interface between the blood and the device, permitting the blood cells to absorb oxygen molecules directly. [7] Click here to see an animation of the basic mechanism of an oxygenator.

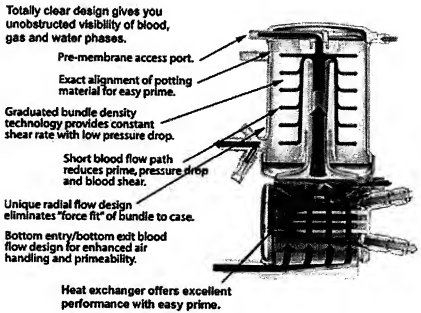
Membrane in an oxygenator allows blood to pass outside rather than inside the fibers. [8] The microporous membranes were hydrophobic polypropylene, which has similar principle as goretex raingear.



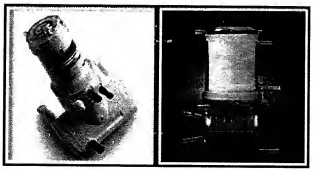
Any blood which escapes the circulation and spills into the operating field around the heart can be suctioned and returned to the pump. This scavenging feature is made possible because the blood has been rendered incapable of clotting by large doses of heparin. Heparin is a powerful anticoagulant

which anticoagulates blood. [9] Once clotting is impaired, a large drainage tube is placed in the upper chamber of the heart (called the right atrium). This tube drains the blue blood from the patient into the heart-lung machine. [10] Then a smaller tube is placed into the arterial system so that red blood can be returned to the patient's body where it is needed. The photograph below illustrates the standard heart-lung tubing (also known as cannulas) after they were inserted into a patient undergoing CABG, but before artificial circulation has been established. [11]

There are several types of oxygenators that are currently used in heart-lung machines. One top selling oxygenator brand worldwide is the Affinity ® NT Oxygenator by Medtronics. The Affinity ® NT Oxygenator is known for being consistent, with its efficient gas transfer, minimized blood shear, low priming volume and low blood side pressure drop. It also has a powerful heat exchanger. [12] The AFFINITY ® NT Oxygenator is available with Trillium ® Biosurface and Carmeda ® * BioActive Surface which are described in other sections.



Along side the Affinity Oxygenator, there is also a pediatric oxygenation system called Minimax Plus ® Oxygenator . This has a unique and efficient fiber geometry which enhances oxygen transfer and can be used to treat a wider range of pediatric patients anywhere from neonates to children. [13] Flow rates can also be varied, as children require a larger flow rate of 2.3 liters/min, than necessary for neonates. [13]



Minimax Plus Oxygenator ———Affinity NT Oxygenator

General areas of improvement:

- Overall biocompatibility between blood and oxygen from oxygenator to improve host homeostasis [14]
- Reduction of systemic anticoagulation [15]
- Better maintanence of platelet count [15]
- Reduction of adhesion of plasma proteins (which would lead to faster formation of blood-friendly secondary superficial membrane) [16]
- Prevention of denaturation and activation of adhered proteins and blood cells [16]
- Avoidance of complication resulting from an abnormal pressure gradient across the oxygenator [16]
- *Improvement of cost of oxygenator [16,17]

last updated 4.30.06